

**Amendments to the Claims**

The following listing of claims replaces all prior versions of the claims pending in this application. Claims 1, 2, 4, 6-16, 20-22, 30, 31, 36-40, 42-44, 48-53, 116-120, 122, and 123 have been amended without any intention of disclaiming equivalents thereof.

**Listing of Claims:**

1. (Currently Amended) A method for preparing ~~nerve tissue for use as~~ a nerve graft, the method comprising:

culturing ~~the~~ a nerve graft comprising a nerve tissue segment *in vitro* under predegenerating conditions that remodel the ~~nerve tissue~~ graft and that increase the neurite-promoting activity of the ~~nerve tissue~~ graft when subsequently implanted ~~the nerve graft is in use~~; and

rendering the ~~nerve tissue~~ graft acellular by killing cells in the ~~nerve tissue~~ graft.

2. (Currently Amended) The method according to claim 1, further comprising performing an *in vitro* neurite outgrowth assay of the ~~nerve~~ graft ~~wherein to determine~~ the increase in neurite-promoting activity ~~is as determined by an~~ *in vitro* neurite outgrowth assay of the ~~nerve~~ tissue.
3. (Original) The method according to claim 2, wherein the *in vitro* neurite outgrowth assay comprises a cryoculture bioassay.
4. (Currently Amended) The method according to claim 1, further comprising performing an *in vivo* neurite outgrowth assay of the ~~nerve~~ graft ~~wherein to determine~~ the increase in neurite-promoting activity ~~is as determined by an~~ *in vivo* neurite outgrowth assay of the ~~nerve~~ tissue.
5. (Cancelled)
6. (Currently Amended) The method according to claim 1, wherein said culturing of the ~~nerve~~ graft *tissue* *in vitro* is for a period of time that achieves an increase in axon ingress and extent of growth within the ~~nerve~~ graft *tissue* when ~~the nerve graft is in use~~ subsequently implanted.

7. (Currently Amended) The method according to claim 1, wherein said culturing of the nerve graft tissue-*in vitro* is for a period of time within the range of about 24 hours to about 96 hours.
8. (Currently Amended) The method according to claim 1, wherein said culturing of the nerve graft tissue-*in vitro* is for a period of time within the range of about 24 hours to about 72 hours.
9. (Currently Amended) The method according to claim 1, wherein said culturing of the nerve graft tissue-*in vitro* is for a period of time of about 48 hours.
10. (Currently Amended) The method according to claim 1, wherein said culturing of the nerve graft tissue-*in vitro* is conducted at a temperature within the range of about 10° C to about 37° C.
11. (Currently Amended) The method according to claim 1, wherein said culturing of the nerve graft tissue-*in vitro* is conducted at a temperature within the range of about 30° C to about 37° C.
12. (Currently Amended) The method according to claim 1, wherein said culturing of the nerve graft tissue-*in vitro* is conducted at a temperature of about 37° C.
13. (Currently Amended) The method according to claim 1, wherein the nerve graft tissue-is an explant.
14. (Currently Amended) The method according to claim 1, wherein the nerve graft tissue-is mammalian tissue.
15. (Currently Amended) The method according to claim 1, wherein the nerve graft tissue-is mammalian tissue selected from the group consisting of human tissue, non-human primate tissue, porcine tissue, rodent tissue, and bovine tissue.
16. (Currently Amended) The method according to claim 1, wherein the nerve graft tissue-is human tissue.
17. (Original) The method according to claim 1, wherein the nerve graft is an autograft.
18. (Original) The method according to claim 1, wherein the nerve graft is an allograft.

19. (Original) The method according to claim 1, wherein the nerve graft is a xenograft.
20. (Currently Amended) The method according to claim 1, wherein rendering the nerve graft tissue-acellular by killing cells in the nerve graft tissue-occurs after culturing.
21. (Currently Amended) The method according to claim 1, wherein rendering the nerve graft tissue-acellular by killing cells in the nerve graft tissue-comprises a process selected from the group consisting of freeze-killing and chemical treatment.
22. (Currently Amended) The method according to claim 1, wherein said method further comprises freezing the nerve graft tissue-for storage.
23. (Original) The method according to claim 22, wherein said freezing is carried out after said culturing *in vitro*.
24. (Cancelled)
25. (Cancelled)
26. (Cancelled)
27. (Cancelled)
28. (Cancelled)
29. (Cancelled)
30. (Currently Amended) The method according to claim 1, wherein the nerve graft tissue-comprises peripheral nerve tissue.
31. (Currently Amended) The method according to claim 1, wherein said culturing comprises placing the nerve graft tissue-in contact with culture medium.
32. (Original) The method according to claim 31, wherein the culture medium comprises a defined medium.
33. (Original) The method according to claim 31, wherein the culture medium comprises a defined medium supplemented with serum.
34. (Original) The method according to claim 31, wherein the culture medium comprises undefined medium.

35. (Original) The method according to claim 31, wherein the culture medium comprises dulbecco's modified eagles' medium.
36. (Currently Amended) The method according to claim 1, wherein said method further comprises isolating the nerve graft tissue-from a mammal prior to said culturing of the nerve graft tissue-in vitro.
37. (Currently Amended) The method according to claim 1, wherein said method further comprises applying a tissue adhesive to the nerve graft tissue.
38. (Currently Amended) A method for enhancing the regenerative potential of nerve tissue for use as a nerve graft, the method comprising:

culturing ~~the~~ a nerve graft comprising a nerve tissue segment *in vitro* under predegenerating conditions that increase the neurite-promoting activity of the nerve graft tissue-when the nerve graft is in use~~subsequently implanted~~, the conditions comprising a temperature within the range of about 10° C to about 37° C for a period of time within the range of about 24 hours to about 96 hours; and

rendering the nerve graft tissue-acellular by killing cells in the nerve graft tissue.
39. (Currently Amended) The method according to claim 38, wherein said culturing of the nerve graft tissue-*in vitro* is for a period of time within the range of about 24 hours to about 72 hours.
40. (Currently Amended) The method according to claim 38, wherein said culturing of the nerve graft tissue-*in vitro* is for a period of time of about 48 hours.
41. (Cancelled)
42. (Currently Amended) The method according to claim 38, wherein said culturing of the nerve graft tissue-*in vitro* is conducted at a temperature within the range of about 30° C to about 37° C.
43. (Currently Amended) The method according to claim 38, wherein said culturing of the nerve graft tissue-*in vitro* is conducted at a temperature of about 37° C.

Amendment and Response to Office Action

U.S. Serial No.: 10/812,776

Atty. Docket No.: AXO-003C1

Page 6 of 20

44. (Currently Amended) The method according to claim 38, wherein said culturing comprises placing the nerve graft tissue-in contact with culture medium.
45. (Original) The method according to claim 44, wherein the culture medium comprises defined medium.
46. (Original) The method according to claim 44, wherein the culture medium comprises defined medium supplemented with serum.
47. (Original) The method according to claim 44, wherein the culture medium comprises undefined medium.
48. (Currently Amended) The method according to claim 38, wherein rendering the nerve graft tissue-acellular by killing cells in the nerve graft tissue-occurs after culturing.
49. (Currently Amended) The method according to claim 38, wherein rendering the nerve graft tissue-acellular by killing cells in the nerve graft tissue-comprises a process selected from the group consisting of freeze-killing and chemical treatment.
50. (Currently Amended) The method according to claim 38, wherein the nerve graft tissue-is mammalian tissue.
51. (Currently Amended) The method according to claim 38, wherein the nerve graft tissue-is mammalian tissue selected from the group consisting of human tissue, non-human primate tissue, porcine tissue, rodent tissue, and bovine tissue.
52. (Currently Amended) The method according to claim 38, wherein the nerve graft tissue-is human tissue.
53. (Currently Amended) The method according to claim 38, wherein the nerve graft tissue-comprises peripheral nerve tissue.
54. (Original) The method according to claim 38, wherein the nerve graft is an autograft.
55. (Original) The method according to claim 38, wherein the nerve graft is an allograft.
56. (Original) The method according to claim 38, wherein the nerve graft is a xenograft.
57. (Withdrawn) A nerve graft comprising nerve tissue prepared by a method comprising culturing the nerve tissue *in vitro* under conditions that permit the nerve tissue to grow *in*

*vitro* and increase the neurite-promoting activity of the nerve tissue when subsequently implanted.

58. (Withdrawn) The nerve graft of claim 57, wherein the increase in neurite-promoting activity is as determined by an *in vitro* neurite outgrowth assay of the nerve tissue.
59. (Withdrawn) The nerve graft of claim 58, wherein the *in vitro* neurite outgrowth assay comprises a cryoculture bioassay.
60. (Withdrawn) The nerve graft of claim 58, wherein the increase in neurite-promoting activity is as determined by an *in vivo* neurite outgrowth assay of the nerve tissue.
61. (Withdrawn) The nerve graft of claim 57, wherein said culturing of the nerve tissue *in vitro* is for a period of time that achieves an increase in axon ingress and extent of growth within the nerve tissue when subsequently implanted.
62. (Withdrawn) The nerve graft of claim 57, wherein said culturing of the nerve tissue *in vitro* is for a period of time within the range of about 24 hours to about 96 hours.
63. (Withdrawn) The nerve graft of claim 57, wherein said culturing of the nerve tissue *in vitro* is for a period of time within the range of about 24 hours to about 72 hours.
64. (Withdrawn) The nerve graft of claim 57, wherein said culturing of the nerve tissue *in vitro* is for a period of time of about 48 hours.
65. (Withdrawn) The nerve graft of claim 38, wherein said culturing of the nerve tissue *in vitro* is conducted at a temperature within the range of about 10° C to about 37° C.
66. (Withdrawn) The nerve graft of claim 38, wherein said culturing of the nerve tissue *in vitro* is conducted at a temperature within the range of about 30° C to about 37° C.
67. (Withdrawn) The nerve graft of claim 38, wherein said culturing of the nerve tissue *in vitro* is conducted at a temperature of about 37° C.
68. (Withdrawn) The nerve graft of claim 57, wherein said nerve tissue comprises living nerve tissue, and wherein said method further comprises rendering the living nerve tissue acellular.

69. (Withdrawn) The nerve graft of claim 57, wherein said nerve tissue comprises living nerve tissue, and wherein said method further comprises freeze-killing the living nerve tissue.
70. (Withdrawn) The nerve graft of claim 57, wherein said method further comprises freezing the nerve tissue for storage.
71. (Withdrawn) The nerve graft of claim 70, wherein said freezing is carried out after said culturing *in vitro*.
72. (Withdrawn) The nerve graft of claim 57, wherein said culturing comprises placing the nerve tissue in contact with culture medium.
73. (Withdrawn) The nerve graft of claim 72, wherein the culture medium comprises defined medium.
74. (Withdrawn) The nerve graft of claim 72, wherein the culture medium comprises defined medium supplemented with serum.
75. (Withdrawn) The nerve graft of claim 72, wherein the culture medium comprises undefined medium.
76. (Withdrawn) The nerve graft of claim 57, wherein the nerve tissue is mammalian tissue.
77. (Withdrawn) The nerve graft of claim 57, wherein the nerve tissue is mammalian tissue selected from the group consisting of human tissue, non-human primate tissue, porcine tissue, rodent tissue, and bovine tissue.
78. (Withdrawn) The nerve graft of claim 57, wherein the nerve tissue is human tissue.
79. (Withdrawn) The nerve graft of claim 57, wherein the nerve tissue comprises peripheral nerve tissue.
80. (Withdrawn) The nerve graft of claim 57, wherein the nerve graft is an autograft.
81. (Withdrawn) The nerve graft of claim 57, wherein the nerve graft is an allograft.
82. (Withdrawn) The nerve graft of claim 57, wherein the nerve graft is a xenograft.
83. (Withdrawn) A method for promoting repair of a damaged nerve comprising implanting a nerve graft at the site of damage, wherein the nerve graft has been prepared by a process comprising culturing the nerve graft *in vitro* under conditions that permit the nerve graft to

grow *in vitro* and increase the neurite-promoting activity of the nerve graft when subsequently implanted.

84. (Withdrawn) The method according to claim 83, wherein said culturing of the nerve graft *in vitro* is for a period of time that achieves an increase in axon ingress and extent of growth within the nerve graft when subsequently implanted.
85. (Withdrawn) The method according to claim 83, wherein the increase in neurite-promoting activity is as determined by an *in vitro* neurite outgrowth assay of the nerve graft.
86. (Withdrawn) The method according to 85, wherein the *in vitro* neurite outgrowth assay comprises a cryoculture assay.
87. (Withdrawn) The method according to 85, wherein the increase in neurite-promoting activity is as determined by an *in vivo* neurite outgrowth assay of the nerve graft.
88. (Withdrawn) The method according to claim 83, wherein said culturing of the nerve graft *in vitro* is for a period of time within the range of about 24 hours to about 96 hours.
89. (Withdrawn) The method according to claim 83, wherein said culturing of the nerve graft *in vitro* is for a period of time within the range of about 24 hours to about 72 hours.
90. (Withdrawn) The method according to claim 83, wherein said culturing of the nerve graft *in vitro* is for a period of time of about 48 hours.
91. (Withdrawn) The method according to claim 83, wherein said culturing of the nerve graft *in vitro* is conducted at a temperature within the range of about 10° C to about 37° C.
92. (Withdrawn) The method according to claim 83, wherein said culturing of the nerve graft *in vitro* is conducted at a temperature within the range of about 30° C to about 37° C.
93. (Withdrawn) The method according to claim 83, wherein said culturing of the nerve graft *in vitro* is conducted at a temperature of about 37° C.
94. (Withdrawn) The method according to claim 83, wherein said nerve graft comprises living nerve tissue, and wherein said process further comprises rendering the living nerve tissue acellular.

Amendment and Response to Office Action

U.S. Serial No.: 10/812,776

Atty. Docket No.: AXO-003C1

Page 10 of 20

95. (Withdrawn) The method according to claim 83, wherein said nerve graft comprises living nerve tissue, and wherein said process further comprises freeze-killing the living nerve tissue.
96. (Withdrawn) The method according to claim 83, wherein said process further comprises freezing the nerve graft for storage.
97. (Withdrawn) The method according to claim 96, wherein said freezing is carried out after said culture *in vitro*.
98. (Withdrawn) The method according to claim 83, wherein said culturing comprises placing the nerve graft in contact with culture medium.
99. (Withdrawn) The method according to claim 83, wherein the culture medium comprises defined medium.
100. (Withdrawn) The method according to claim 83, wherein the culture medium comprises defined medium supplemented with serum.
101. (Withdrawn) The method according to claim 83, wherein the culture medium comprises undefined medium.
102. (Withdrawn) The method according to claim 83, wherein the nerve graft is mammalian tissue.
103. (Withdrawn) The method according to claim 83, wherein the nerve graft is mammalian tissue selected from the group consisting of human tissue, non-human primate tissue, porcine tissue, rodent tissue, and bovine tissue.
104. (Withdrawn) The method according to claim 83, wherein the nerve graft is human tissue.
105. (Withdrawn) The method according to claim 83, wherein the nerve graft comprises peripheral nerve tissue.
106. (Withdrawn) The method according to claim 83, wherein the damaged nerve comprises nerve tissue of the central nervous system.

107. (Withdrawn) The method according to claim 83, wherein said method further comprises applying a tissue adhesive to the damaged nerve, or to the nerve graft, or to both the damaged nerve and the nerve graft.
108. (Withdrawn) The method according to claim 83, wherein the nerve graft is a terminal nerve graft.
109. (Withdrawn) The method according to claim 83, wherein the nerve graft is an interpositional nerve graft.
110. (Withdrawn) The method according to claim 83, wherein said method further comprises applying at least one chondroitin sulfate proteoglycan-degrading enzyme to the damaged nerve, or the nerve graft, or both the damaged nerve and the nerve graft.
111. (Withdrawn) The method according to claim 110, wherein the chondroitin sulfate proteoglycan-degrading enzyme is applied to the nerve graft after said culturing *in vitro*.
112. (Withdrawn) The method according to claim 83, wherein said method further comprises resecting the damaged nerve prior to said applying of the nerve graft.
113. (Withdrawn) The method according to claim 83, wherein the nerve graft is autologous with the damaged nerve.
114. (Withdrawn) The method according to claim 83, wherein the nerve graft is allogeneic with the damaged nerve.
115. (Withdrawn) The method according to claim 83, wherein the nerve graft is xenogeneic with the damaged nerve.
116. (Currently Amended) A method for preparing ~~nerve tissue for use as a~~ nerve graft, the method comprising:

placing ~~the~~ a nerve graft comprising a nerve tissue segment in conditions *in vitro* that are permissive to the activation and proliferation of cells within the nerve graft tissue, are permissive to the activity of enzymes produced by cells within the nerve graft tissue, are permissive to the degeneration and remodeling of the nerve graft tissue *in vitro*, and increase the neurite-promoting activity of the nerve graft tissue when the nerve graft is in use subsequently implanted; and

Amendment and Response to Office Action

U.S. Serial No.: 10/812,776

Atty. Docket No.: AXO-003C1

Page 12 of 20

rendering the nerve graft acellular by killing cells in the nerve graft.

117. (Currently Amended) The method according to claim 1, wherein the nerve graft tissue comprises central nervous system tissue.
118. (Currently Amended) The method according to claim 38, wherein the nerve graft tissue comprises central nervous system tissue.
119. (Currently Amended) The method according to claim 38, wherein the nerve graft tissue is an explant.
120. (Currently Amended) The method according to claim 38, wherein said method further comprises freezing the nerve graft tissue for storage.
121. (Previously Presented) The method according to claim 120, wherein said freezing is carried out after said culturing *in vitro*.
122. (Currently Amended) The method according to claim 38, wherein said method further comprises isolating the nerve graft tissue from a mammal prior to said culturing of the nerve graft tissue *in vitro*.
123. (Currently Amended) The method according to claim 38, wherein said method further comprises applying a tissue adhesive to the nerve graft tissue.